

REMARKS

In the present communication, claim 1 has been amended; claims 20-24, 26-33, 35-38 and 40-41 have been canceled without prejudice or disclaimer; and claim 42 has been added. The amendments and new claims do not add new matter and are fully supported throughout the specification and claims as filed as discussed below. Accordingly, upon entry of the present amendment claims 1, 3-10, 12-14, 16-18, 39 and 42 will be pending and at issue.

Applicants thank the Office for the Interview conducted on January 11, 2010. Further, Applicants respectfully request that upon consideration of the present amendments, if the claims are not deemed allowable, a non-final action be issued as a Request for Continued Examination is submitted herewith.

Amendments to the Claims

Various amendments have been made to the claims as provided herein. The amendments are fully supported throughout the specification and claims as filed and do not add new matter. Support for the amendments are provided below as identified in the application as published in U.S. Patent Application Publication 2006/0151900.

Claim 1 has been amended to clarify that the homogeneous solution formed by equilibrating the molten substance and the liquefied or dense gas is contacted by a carrier fluid such that the carrier fluid is passed through the solution to pass that solution from the pressure chamber through the outlet into a vessel of lower pressure to form particles of the substance. Support for the amendment may be found throughout the specification, for example, in paragraphs [0076] and [0077]. Accordingly, no new matter has been introduced.

New claim 42 has been added to specify that the solution is passed by the carrier fluid from the pressure chamber through the outlet into a vessel of lower pressure via a pre-pressurized nozzle. This is to prevent a pressure drop and particle formation before the nozzle to avoid blockage of the nozzle. Support for the amendment may be found throughout the specification, for example, in paragraph [0076].

Rejections under 35 U.S.C. §103

Applicants respectfully traverse the rejection of claims 1, 3-6, 8-12 and 39 under 35 U.S.C. §103(a) as allegedly being obvious over Kerč et al. (*International Journal of Pharmaceuticals*, 182:33-39 (1999); hereinafter “Kerč”) in view of Kropf et al. (U.S. Patent No. 6,316,030; hereinafter “Kropf”), Jung et al. (*Journal of Supercritical Fluids*, 20:179-219 (2001); hereinafter “Jung”), and Weidner et al. (U.S. Patent No. 6,056,791; hereinafter “Weidner”).

The U.S. Supreme Court decision in *KSR International v. Teleflex Inc.* (82 USPQ2d 1385), modified the standard for establishing a *prima facie* case of obviousness. Under the *KSR* rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references still has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references.

Without acquiescing to the reasoning presented in the Office Action, and in order to expedite prosecution of the instant application, Applicants have amended claim 1 to further clarify that the homogeneous solution formed by equilibrating the molten substance and the liquefied or dense gas is contacted by a carrier fluid such that the carrier fluid is passed through the solution to pass the solution from the pressure chamber through the outlet into a vessel of lower pressure to form particles of the substance. The Office Action acknowledges that Kerč fails to disclose a method utilizing a pressure chamber having an outlet that is above an inlet as well as use of a carrier fluid at the same pressure as the liquefied gas to pass the molten homogeneous solution out through the outlet. The Office Action points to Jung and Weidner to remedy the deficiencies.

Kerč, Kropf and Weidner pertain to a process known as ‘Particles from Gas Saturated Solutions’ (PGSS) in which a gas is dissolved under pressure in a melted drug which is later

expanded resulting in particle precipitation. Jung pertains to a Gas Anti-Solvent (GAS) process as opposed to the PGSS process. One of skill in the art would appreciate the differences in the two processes, especially as regards formation of fine particles. For example, the GAS process described by Jung includes introducing a compressed gas into the bottom of a precipitator vessel partially filled with a batch of solution including a liquid solvent having solute (*e.g.*, drug) dissolved therein. The solution is expanded by introduction of a compressed gas anti-solvent, in which the mixture becomes supersaturated and solute precipitates out of solution (page 187, column 2 to page 188, column 1). Unlike in a typical PGSS process in which particles are formed by spraying a molten gas/drug solution, Jung describes that after expansion of the solution in the GAS process by introduction of the compressed gas (anti-solvent), the batch of expanded solution is held in the precipitator vessel for a period of time, after which the expanded solution is drained and the precipitated particles cleaned (page 188, column 1, lines 6-9). Thus, one skilled in the art would understand that the compressed gas of Jung identified in the passage cited in the Office Action is not a carrier gas as used in a PGSS process since the gas does not carry particles of the solution through an outlet to form particles in a continuous process as in a PGSS process or that claimed.

Similarly, one skilled in the art would understand that the compressed gas of Jung is not a carrier gas as used in the presently claimed method termed 'Particles from Dense Gas Induced Molten Solutions' (PDGIMS), in which a carrier gas is contacted with a pressurized gas saturated solution and carries the gas saturated solution through a nozzle resulting in expansion of the gas. Unlike the GAS process disclosed in Jung or the typical PGSS process of Kerč, Kropf or Weidner, in the method of the amended claims (*e.g.*, the PDGIMS process), the molten homogeneous solution formed by a substance being melted by a dense or liquefied gas, is contacted with a carrier fluid which may also be a dense or liquefied gas and introduced to the pressure chamber through the inlet which is positioned below the outlet and at the bottom of the pressure chamber containing the homogeneous solution including the molten substance. The carrier fluid is passed through the molten homogeneous solution and exits the chamber at a

higher point through an outlet, having taken at least a part of the molten homogeneous solution with it.

The Office Action alleges that it would have been obvious to one skilled in the art to use the inlet/outlet configuration of Jung in the method of Kerč. Applicants disagree. As discussed above, the GAS process disclosed in Jung fails to include a carrier gas as in a typical PGSS process. Further, Applicants assert that the rationale for introduction of the compressed anti-solvent gas to the bottom of the precipitation vessel in the GAS method of Jung is different than for a PGSS process and not applicable to PGSS or PDGIMS of the present claims since the compressed anti-solvent gas is not a carrier fluid. In Jung, the compressed anti-solvent gas is introduced to expand the solvent/solute solution in the vessel, as opposed to use as a carrier. One skilled in the art would not be motivated to apply the alleged teaching of Jung to that of Kerč, or Kropf or Weidner, to arrive at the claimed invention given the clear differences in the GAS process as compared to the claimed process regardless of the assertion that one would apply the teachings of Jung in practicing the method of Kerč to achieve better mixing of the carrier gas and solution. However, as discussed in the specification, one skilled in that art would appreciate that better mixing is not a valid motivation since having the inlet disposed beneath the outlet "is to deliberately keep the liquefied gas or dense gas solution below saturation. This assists in avoiding blockages in the 50 micron nozzle." (See end of paragraph [0077] of the specification). Thus the molten homogeneous solution is advantageously less viscous (see paragraphs [0049] and [0050] of the specification) which assists in preventing blockage of the outlet nozzle.

Given that the GAS process described in Jung fails to utilize a carrier gas as opposed to the PGSS method of Kerč, Kropf and Weidner, and Jung further fails to provide any guidance as to introduction of carrier gases into the bottom of a vessel to carry a gas saturated solution through an outlet disposed above the inlet, one skilled in the art would not be motivated to combine the teachings of Jung with those of Kerč, Kropf or Weidner to arrive at the claimed invention. Further, a highlight of the presently claimed process is that it avoids use of organic solvents (see paragraph [0051] of the specification), such as those typically used in the GAS

process of Jung. Thus one skilled in the art would not be motivated to combine the teachings of Kerč, Kropf or Weidner with those of Jung to arrive at the claimed invention.

Furthermore, the standard PGSS ('Particles from Gas-Saturated Solutions') apparatus known by one skilled in the art at the time of filing was configured such that the inlet for supplying the carrier gas to the vessel containing the molten solution is not below the outlet as claimed (see paragraph [0077] of the specification; and column 8, lines 18-21 of Weidner). This is so that the carrier gas is not introduced into the bottom of the vessel as claimed, but rather into the top of the vessel (column 8, lines 18-21 of Weidner). Given the standard configuration of PGSS apparatuses, one of skill in the art would not appreciate the unexpected advantages of providing the outlet above the inlet such that the carrier gas is introduced at the bottom of the vessel and passes through the molten homogenous solution as claimed, such as keeping the liquefied gas or dense gas solution below saturation to avoid blockages in the outlet nozzle.

It is axiomatic that one cannot simply use the Applicants' disclosure as a "blueprint" to reconstruct, by hindsight, Applicants' claim (*see, e.g., Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985)). As there is provided no motivation to combine the references, no *prima facie* case of obviousness has been established. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Applicants respectfully traverse the rejection of claims 7, 14 and 16-18 under 35 U.S.C. §103(a) as allegedly being obvious over Kerč in view of Kropf as applied to claims 1 and 6, and further in view of Zhu et al. (US 2002/0110526; hereinafter "Zhu").

As discussed above, without acquiescing to the reasoning presented in the Office Action, and in order to expedite prosecution of the instant application, Applicants have amended claim 1 to further clarify that the homogeneous solution formed by equilibrating the molten substance and the liquefied or dense gas is contacted by a carrier fluid such that the carrier fluid is passed through the solution to pass the solution from the pressure chamber through the outlet into a vessel of lower pressure to form particles of the substance.

Further as discussed above and acknowledged in the Office Action, Kerč fails to disclose a method utilizing a pressure chamber having an outlet that is above an inlet as well as use of a carrier fluid at the same pressure as the liquefied gas to pass the molten homogeneous solution out through the outlet. Kropf also fails to disclose such a method. Applicants note that in the rejection of claims 1, 3-6, 8-12 and 39 as allegedly obvious which is addressed above, the Office Action points to Jung and Weidner to remedy these deficiencies. Therefore, as pertains to the rejection of claims 7, 14 and 16-18, citing Kerč, Kropf and Zhu, the Office Action fails to present a *prima facie* case of obviousness, since the cited references, alone or in combination, fail to teach each and every element of the claimed invention. Accordingly, withdrawal of the rejection is respectfully requested.

As this rejection may be presented further citing Jung and Weidner as addressed above, Applicants provide the following arguments. In addressing the teachings of Kerč, Kropf, Jung and Weidner above, given the differences in the GAS process of Jung with the PGSS process of Kerč, Kropf and Weidner one skilled in the art would not be motivated to combine the teachings of the references to practice the claimed invention. Further, since the GAS process described in Jung fails to utilize a carrier gas as opposed to the PGSS method of Kerč, Kropf and Weidner, and Jung further fails to provide any guidance as to introduction of carrier gases into the bottom of a vessel to carry a gas saturated solution through an outlet disposed above the inlet, one skilled in the art would not be motivated to combine the teachings of Jung with those of Kerč, Kropf or Weidner to arrive at the claimed invention. Applicants assert that Zhu further fails to provide any motivation to combine the references to arrive at the present invention utilizing a vessel including an inlet that is below an outlet. Zhu generally pertains to slow-released coated particles and provides no teachings or guidance as to particular PGSS or GAS processes. As there would be no motivation to combine the references, no *prima facie* case of obviousness may be established, and the claimed invention is not rendered obvious by the prior art.

Conclusion

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

The Commissioner is hereby authorized to charge the total amount of \$960.00 to cover the payment of a Request for Continued Examination fee, small entity (\$405.00) and a Three-Month Extension of Time fee, small entity (\$555.00) to Deposit Account No. 07-1896. No other fees are deemed necessary with the filing of this paper. However, the Commissioner is further authorized to charge any additional fees, or credit any overpayments, to Deposit Account No. 07-1896 referencing the above-identified docket number.

Respectfully submitted,

Date: January 19, 2010


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